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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/829,481	04/10/2001	James K. Presnail	BB1441USNA	8059

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ALSTON & BIRD LLP
PIONEER HI-BRED INTERNATIONAL, INC.
BANK OF AMERICA PLAZA
101 SOUTH TYRON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER	
KUBELIK, ANNE R	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 05/20/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

14 § ~ 1449

Office Action Summary	Application No.	Applicant(s)	
	09/829,481	PRESNAIL ET AL.	
	Examin r	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,12-16,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,12-16,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment of claims 1-2, 14 and 22, and the addition of claim 23 requested in Paper No. 13, filed 21 February 2003, have been entered. Claims 1-8, 12-16 and 22-23 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. Claims 1-8, 12-16 and 22-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 21 November 2002, as applied to claims 1-8, 12-16 and 22. Applicant's arguments filed 21 February 2003 have been fully considered but they are not persuasive.

Applicant urges that the specification teaches defensin encoding nucleic acids from *Scolopendra canidens* and *Argiope*, as well as *Vaejovis carolinianus*. Applicant urges that SEQ ID NO:4 is a cationic peptide and contains all the conserved cysteine residues found in insect defensins, as shown in Appendix A. Applicant also urges that SEQ ID NO:4 has a high degree of similarity with the Arthropod defensin consensus sequence, as shown in Appendix B. Applicant cites Bulet et al and Cho et al but does not send them (response pg 3-5).

This is not found persuasive. It is not clear in Appendix A what the sequences in the lower portion are. Appendix B contains little textual explanation - for example, what is the significance of the capital letters vs the lower case letters in the alignment? What do the plus

signs mean? Thus, Appendix A and B could not be evaluated. Bulet et al and Cho et al could not be considered because they were not sent.

Applicant urges that the USPTO accepts sequence homology as a basis for establishing utility and that this rejection is typically made under both 35 USC 101 and 35 USC 112. Applicant urges that the Utility guidelines make it clear that sequence homology is sufficient to establish utility and that working examples are not required for establishment of utility. Applicant urges that nucleic acids encoding defensins have a well-established utility, comparable to ligase in the Utility Guideline Training Materials Example 10 (response pg 6-7).

This is not found persuasive. This is a rejection made under 35 USC 112, so Applicant's arguments regarding the Utility Training Guidelines are moot. It is noted that considerations for evaluating the claims under 35 USC 112 are different than those made for evaluating the claims under 35 USC 101.

Applicant urges that the prior art discusses defensin gene families from a wide array of organisms and they have similarities from 58% to 95%. Applicant urges that assays performed on proteins with these properties have confirmed that they have defensin activity. Applicant cites Bulet et al, Cho et al, White et al, Broekaert et al, Lamberty et al, Thevissen et al, and Terras et al. Applicant urges that one of skill in the art would accept that SEQ ID NO:4 functions as a defensins (response pg 7-8).

This is not found persuasive because. Of the references cited, only Terras et al, cited in the IDS filed 30 May 2001, could be considered; the others were not sent. Terras et al is directed toward a radish anti-fungal peptide and presents no comparisons to Arthropod defensins.

Without the other supporting documents, Applicant's arguments are assertions only, and do not overcome the rejection.

Applicant urges that there are several critical differences between the instant inventions and Pang et al and Barton et al, cited in the prior Office action. Applicant urges that these studies sought to control large insect predators, while defensins protect against pathogens, including Gram-positive bacteria. Applicant cites Boman et al, White et al, Cho et al, Bulet et al and Hetru et al. Applicant urges that while the defensins of the instant invention may also provide protection against insect pathogens, some defensins protect against fungal and bacterial infection; Applicant cites Terras et al and Brockaert et al. Applicant urges that the fact that the Pang and Barton studies could not control insects using non-defensin proteins is irrelevant and numerous studies have demonstrated the efficacy of defensins against a wide array of bacterial and fungal pathogens (response pg 8-10).

This is not found persuasive. Of Boman et al, White et al, Cho et al, Bulet et al, Hetru et al, Terras et al and Brockaert et al, only Terras et al, cited in the IDS filed 30 May 2001, could be considered; the others were not sent. The protein described by terras et al was not transgenic ally expressed in a plant, and thus has no relevance to the portion of the enablement rejection directed to unpredictability of expression of these proteins in plants.

Applicant's arguments with respect to Pang et al and Barton et al are off topic. These references were discussed in the rejection because they show that when small proteins are expressed in plants they may unexpectedly not work, even though the isolated protein was quite effective. In the case of Pang et al, this occurred because the protein was not correctly processed

(pg 170, right column). The specification does not overcome this unpredictability by showing that SEQ ID NO:3 can be effectively expressed in a plant to produce a functional protein.

Applicant urges that one of skill in the art, using the guidance presented in the specification, could make and use the claimed invention, and urges that the specification provides guidance for determining percent identity of sequences. Applicant also urges that claim 1 specifies that the protein has defensin activity and thus encompasses functional variants. Applicant states that Terras et al, Oh et al, Thevissen et al (1996), and Thevissen et al (1999) and Lamberty et al teach defensin assays. Applicant urges that thus guidance is provided as to which region of SEQ ID NO:4 can be altered and that the claimed sequences can vary by structural parameters and are required to retain defensin activity (response pg 10-11).

This is not found persuasive. Of the references cited, only Terras et al and Thevissen et al (1996), cited in the IDS filed 30 May 2001, could be considered; the others were not sent. Neither Terras et al nor Thevissen et al teach modification of defensins; the rejection was not a lack of enablement for methods of assaying defensins. Applicant did not point to guidance in the specification for which regions of SEQ ID NO:4 can be altered; guidance for calculating percent identity is not the same as guidance for making amino acid substitutions that result in a protein with a specified activity. Which amino acids of SEQ ID NO:4 are essential for defensin activity and which can be altered, and to what other amino acids?

Applicant urges that undue experimentation would not required to make and use the claimed invention, and cites *In re Wands* and *In re Jackson*, which states that experimentation is permissible. Applicant urges that shuffling to make and assay a number of sequences is taught in US Patent 5,837,458. Applicant also cites Minshull et al and Christains et al. Applicants states

that *In re Wands* only considered the experimentation required to identify one or few monoclonal antibodies with the required affinity and *Johns Hopkins vs Cellpro* states that only one mode of making the claimed invention need to enabled. Applicant urges that guidance for making a nucleic acid with the applicable limitation of the claims and assaying the encoded protein is provided in the specification (response pg 11-13).

This is not found persuasive because the specification does not teach the critical amino acids of SEQ ID NO:4. The specification teaches no nucleic acids that encode proteins with 90% identity to SEQ ID NO:4, and it is not clear that SEQ ID NO:4 is a defensin, as discussed above. None of the cited references could be considered because they were not sent.

4. Claims 1-8, 12-16 and 22-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 21 November 2002, as applied to claims 1-8, 12-16 and 22. Applicant's arguments filed 21 February 2003 have been fully considered but they are not persuasive.

Applicant urges that claim 1 requires that the protein has defensin activity and that it have 90% identity to SEQ ID NO:4. Applicant urges that recitation of at least 90% sequence identity is a very predictable structure. Applicant urges that all that is required is disclosure of a representative number of the claimed sequences, not individual support for each species of a claimed genus. Applicant urges that a genus of DNAs may be claimed by recitation of structural

features common to the genus, and functional characteristics may be relied on ; Applicant urges that claim 1 recites the functional characteristics of the claimed genus (response pg 13-14).

This is not found persuasive. It is agreed that the structure of nucleic acids that encode proteins with 90% identity to SEQ ID NO:4 is very predictable. However, the structure of nucleic acids that encode proteins with 90% identity to SEQ ID NO:4 and that encode a protein with defensin activity is not. The specification does not describe the structural features (*i.e.*, sequence) of even one such nucleic acid.

Applicant urges that Example 14 of the Written Description Guidelines states that claim to a protein with 95% sequence identity to a sequence identifier and that recites the reaction catalyzed by the protein meets the written description requirement; thus, Applicant urges the instant claims also meet the Written Description Guidelines (response pg 14-15).

This is not found persuasive because the claims are drawn to nucleic acids that encode proteins with **90%** identity to SEQ ID NO:4; thus, they do not fit the scenario in Example 14 of the Written Description Guidelines.

Applicant urges that *Eli Lilly* and *Amgen* do not apply to the present situation because structural and functional definitions are provided (response pg 15-16).

This is not found persuasive because the specification does not describe the structural features (*i.e.*, sequence) of nucleic acids that encode proteins with 90% identity to SEQ ID NO:4.

5. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

Claim 22 lacks antecedent basis for the limitation "said cells" in line 4.

6. Claims 1-8, 12-16 and 22 are free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid encoding a protein with at least 80% identity to SEQ ID NO:4.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
May 8, 2003

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600